GPIIb/IIIa inhibitors exert their inhibitory effect through RGD-mediated interactions. We have recently synthesized a constraint cyclic peptide, (S,S) PSRCDCR-NH_2, that exhibits potent non-RGD antiplatelet activity in vitro. The effects of the peptide on a rabbit experimental thrombosis model are investigated.
Methods: Three groups (n=5 animals in each group) received: i) normal saline, 6ml/kg/h (control group), ii) (S,S) PSRCDCR-NH_2, 6 mg/kg bolus plus 2.4 mg/kg/h, and iii) eptifibatide, 900 µg/kg bolus plus 10 µg/kg/h. Carotid artery thrombus formation was induced by electrical stimulation, under continuous blood flow monitoring, in all animals. Ex vivo platelet aggregation to 20 µM ADP and 500 µM AA in platelet rich plasma (PRP) was determined before (baseline) and at 60 min after the initiation of drug administration (instantly prior to electrical stimulation). At 90 min after electrical stimulation the carotid thrombus was removed and weighed. Blood loss was calculated by the amount of blood, gathered on a pre-weighed gauze, positioned on a standardized incision performed on the anterior abdominal wall.
Results: In the control group, carotid artery was totally occluded within 23.3±3.2 min after electrical stimulation, while in the (S,S) PSRCDCR-NH_2 and eptifibatide groups, carotid artery blood flow at 90 min after electrical stimulation, was reduced to 45.9±1.5% and 35.3±2.0% respectively ($p<0.001$ vs control). Thrombus weight was significantly reduced in animals receiving (S,S) PSRCDCR-NH_2 or eptifibatide vs control (1.5±0.3mg or 2.1±1.1mg vs 5.7±0.8mg, respectively, $p<0.008$ vs control). Platelet maximum aggregation to ADP and AA in the control group was not altered 60 min after electrical stimulation compared to baseline, whereas it was significantly inhibited in the (S,S) PSRCDCR-NH_2 and eptifibatide groups to ADP [by 42.1±3.1 and 38.3±11.0% ($p<0.005$ vs control)], and to AA [by 75.6±12.0 and 40.0±11.1%, ($p<0.007$ vs control)]. No significant increase of blood loss was observed in (S,S) PSRCDCR-NH_2 and eptifibatide groups compared to control.
Conclusions: (S,S) PSRCDCR-NH_2, a non-RGD novel cyclic peptide, reduces experimental thrombus formation in a rabbit carotid artery thrombosis model by inhibiting platelet aggregation without affecting bleeding assays.

TCT-131

Influence of Heart Rate on Diagnostic Parameters for Epicardial Coronary Stenosis with Concomitant Microvascular Disease

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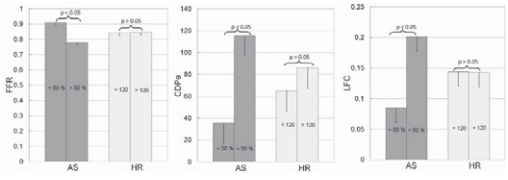
Background: Presence of concomitant microvascular disease (MVD) affects the diagnosis of epicardial stenosis (ES) during cardiac catheterization. The diagnosis is also affected by factors like heart rate (HR) and percentage area stenosis (AS). For better diagnosis, this study evaluates the influence of HR on fractional flow reserve (FFR) and alternative diagnostic indices, pressure drop coefficient (CDPe) and lesion flow coefficient (LFC), for various degrees of ES with MVD. We hypothesize that FFR, CDPe, and LFC, assessed in vivo, are independent of HR.
Methods: Simultaneous measurements of hyperemic coronary-arterial pressure drop (dp) and average peak flow velocity (APV) were performed on 10 pigs (52±5 kg), using a dual sensor-tipped guidewire. ES and MVD were created using angioplasty balloons and 90 µm polystyrene microspheres, respectively. Vessel area was measured using IVUS catheter. CDPe and LFC were calculated as (dp)/(0.5*1.05*APV²) and , respectively; k is (1-AS) and u_m is the velocity at the site of stenosis. FFR, CDPe and LFC were assessed for "AS<50%" and "AS>50%", for HR<120 and HR>120 bpm. A 2-way repeated measure ANOVA was performed with 500 measurements to determine the influence of HR on diagnostic parameters for variable AS with MVD. $p < 0.05$ was considered statistically significant.
Results: The mean values of FFR (0.84±0.02 for both HR <120, >120), CDPe (65.11±18.93: HR<120, 86.16±18.9: HR>120), and LFC (0.14±0.02 for both HR< 120, >120) were not significantly different ($p>0.05$) for variable HR conditions. The mean values of FFR (0.90±0.02: AS <50%, 0.78±0.01: AS >50%), CDPe (35.80±19.10: AS<50%, 115.48±18.25: AS>50%), and LFC (0.09±0.02: AS<50%, 0.20±0.02: AS>50%) were significantly different ($p<0.001$) under variable AS conditions.



Conclusion: For ES with concomitant MVD, HR has insignificant influence on FFR, CDPe, and LFC.

TCT-132

Impact of Orientation and Size Matched Transcatheter Aortic Valves on Valve-in-Valve Hemodynamics

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Background: Transcatheter aortic valve implantation (TAVI) is a viable treatment for selected patients with failing bioprosthesis. We have previously shown that currently available SAPIEN TAV sizes did not yield acceptable valve-in-valve hemodynamics in small degenerated bioprostheses, since optimal TAV function required full stent expansion to its nominal size. The study objective was to determine if a 20mm TAV provides acceptable hemodynamics in small degenerated bioprostheses and the impact of TAV spatial orientation on valvular hemodynamics and coronary flows.
Methods: 20mm TAVs were created for TAVI within 19 and 21mm degenerated PERIMOUNT bioprostheses. Bioprosthetic degeneration was simulated using BioGlue to yield a consistent 50mmHg mean gradient. Degenerated valves sutured into human homograft roots were mounted in a pulse duplicator. TAVI within bioprostheses was oriented with TAV and commissures aligned and then rotated 60º.
Results: 20mm TAVs in 21mm bioprostheses migrated retrograde into the left ventricle, whereas TAVI in 19mm bioprostheses significantly reduced mean gradients (Table 1). Mild regurgitation was seen and energy loss was significantly higher than with surgical re-replacement using normal 19mm valves. TAVI orientation had no impact on hemodynamics or coronary flows.

Table 1. Hemodynamics before and after TAVI in 19mm degenerated PERIMOUNT compared with normal 19mm bioprosthesis.

	Degenerated 19mm Bioprosthesis	Valve-in-Valve (commissures aligned)	Valve-in-Valve (60º rotated)	Normal 19mm Bioprosthesis
Pressure Gradient (mmHg)	54.9±5.4	23.5±3.9*	25.2±5.4*	11.5±2.0†
Effective Orifice Area (cm^2)	0.69±0.03	1.07±0.10*	1.04±0.14*	1.54±0.13†
Regurgitation Fraction (%)	3.7±1.8	16.8±2.4*	16.9±0.4*	4.8±1.7†
Total Energy Loss (mJ/stroke)	809.0±52.1	582.3±27.5*	610.0±74.7*	248.7±23.9†

* is p<0.04 between degenerated bioprostheses and valve-in-valve.
† is p<0.05 between valve-in-valve (both orientations) and normal bioprosthesis.

Conclusions: Valve-in-valve hemodynamics for 19mm degenerated bioprostheses improved with size specific TAVs which match bioprosthetic size. TAVI orientation within bioprostheses did not affect hemodynamics.

TCT-133

A Time-course Study of Vasomotor Function After Implantation of Novel Paclitaxel-eluting Stent in Rabbit Iliac Arteries

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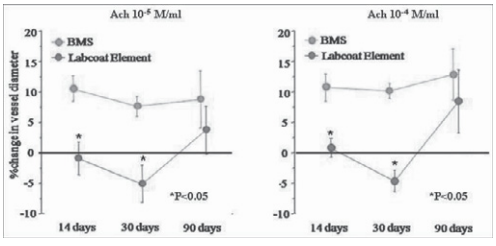
Background: A growing body of clinical data has shown that the 1st-gen of paclitaxel-eluting stents (PES) implantation could lead to vasomotor dysfunction. Novel generation of PES (Labcoat) has much less drug in combination with abluminal biodegradable polymer coating that eventually leave a polymer-free BMS when drug is gone. In this study, we aimed to investigate the time-course changes of vasomotor function following implantation of a novel PES in rabbit iliac arteries.
Methods: BMS (Element, n=18) and Labcoat Element (Labcoat, n=18, about 10-fold less drug than the 1st-generation of TAXUS) were implanted at rabbit iliac arteries. Endothelial function at 5-10 mm distal to the stents was estimated by acetylcholine (Ach 10^{-5}, 10^{-4} M/mL) infusion at 14d, 30d, and 90d (6 animals per time-point).
Results: Arteriographic minimal luminal diameter, as well as percent diameter stenosis, was not different between two groups ($P>0.05$). Decreased vasodilatory response for Labcoat group was found at earlier time points (14, 30d) when compared to BMS (Labcoat vs. BMS, Ach 10^{-5}; -0.92±6.37% vs. 10.5 ±5.93%, Ach10^{-4}; 0.81±3.96% vs. 10.72±6.30% at 14 days, $p<0.01$, respectively, Ach 10^{-5}; -5.08±7.58% vs. 7.58±4.09%, Ach10^{-4}; -4.61±4.30% vs. 10.17±3.03% at 30 days, $p<0.01$, respectively). However, at 90d, the vasomotor function response to Ach was not different between the two groups (Labcoat vs. BMS, Ach 10^{-5}; 3.76±9.53% vs. 8.79±11.49%, Ach 10^{-4}; 8.49±12.59% vs. 12.81±10.32%, p=NS, respectively).



Conclusions: In vivo evaluation of the early and long-term safety after drug-eluting stent placement is important in clinical setting. Our results demonstrated that comparable endothelial function of BMS and Labcoat stented vessels was reached within three months post stent implantation, which may indicate completion of drug release and healing process.

TCT-134

Coronary Bifurcation Lesions Treated with the Novel Advanced Bifurcation SystemsTM Dedicated Stent: Animal Experience

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Background: Current dedicated bifurcation stent systems are limited in their efficacy. The ABS Modular Bifurcation System (Advanced Bifurcation Systems, Los Angeles CA) is a novel stent platform designed for automatic alignment and orientation of the main branch and side branch stents with complete coverage of the carina and side-branch access. The ABS device is a modular, dual-catheter, independently movable stent delivery system (currently 7f). It consists of a mother-daughter stent (MD) on an over-the-wire balloon catheter and a daughter stent (DS) on a monorail catheter. The DS catheter is loaded on a sleeve of the MD catheter and protrudes through an opening in the middle of the MD stent and leads the system. The DS delivery balloon is twice the length of the DS which is mounted on the distal half of this balloon.
Methods: The system is loaded on 2 wires and advanced until it reaches the carina. The leading DS catheter is then pulled back into the MD stent so that the proximal markers of the two balloons are aligned. The bifurcation stent is now assembled at the carina. The DS balloon is inflated first and partially deploys and rotates the proximal segment of the MD to align with the daughter vessel automatically. It simultaneously deploys the DS. The MD balloon is inflated to deploy the MD stent. Kissing balloon inflation fully deploys the system.
The ABS System was implanted in 2 sets of porcine models. The first group underwent 3 implants each and were euthanized immediately. Their hearts were studied for implant characteristics. The second group of pigs underwent 1 implant each and underwent a 45-day follow-up angiogram.

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